Title of project: Neuroendocrine Lung Cancer: Mechanistic studies

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Abstract

Lung cancer is the most frequent cause of death from cancer in man. There are two major forms of human lung cancer: small cell and non-small cell cancer. The successful prevention and treatment of lung cancer will eventually be based on a knowledge of the molecular and cellular events underlying the pathogenesis of this disease. Understanding of oncogene expression is a crucial step in such a development. We propose to analyze oncogene expression in non-small cell lung cancers induced in hamsters by a lung-specific nitrosamine and in small cell lung cancers produced by concomitant exposure of hamsters to a nitrosamine and hyperoxia; treatment regimens will be used that induce tumors within a comparatively short time period (3 to 4 months) and with high incidence (70% to 80%). Hamster-specific probes will de developed and oncogene expression will be evaluated during tumor development and in the tumors that eventually form. We hypothesize that oncogene expression (ras, myc) and/or tumor suppressor inactivation (Rb, p53) is an obligatory early event in development of lung tumors. Thus, we predict that there will be characteristic patterns of oncogene expression for both tumor types to be studied herein. These early patterns of gene expression will allow for accurate prediction of ultimate tumor type.Analysis of neuroendocrine cell proliferation in lung tissue of hamsters exposed to a carcinogenic regimen will serve as an additional quantitative and qualitative indicator of lung tumor development.

Signature, Principal Investigator

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